cells and, in particular, it is noted in Dr. Gruber's Declaration in adults there will not be any nucleus cells.

As previously noted, in early childhood the intervertebral disc consists of a peripheral annulus and a central nucleus. The intervertebral disc and particularly its nucleus undergo continuous change during development, maturation, and degeneration. The nucleus disappears in early childhood and becomes fibrocartilaginous in adolescents and adults. The annulus becomes almost avascular in adults. *See*, Taylor and Twomey, "*The development of the human intervertebral disc.*" Chap.2 in Vol.1., p. 40, The Biology of the Intervertebral Disc., P.Ghosh, ed. CRC Press, Boca Raton, FL. 1988). The specification discusses the use of annulus and nucleus cells in this invention and while annulus cells have been used it would not matter if there were a few cells from the nucleus region of the disc. *See Specification, page 5, lines 13-14.*

The Examiner next questions whether the cells in the therapeutic composition are de-differentiated, proliferating cells, or whether the cells are differentiated and secreting an extra cellular matrix that is representative of the matrix observed in a normal intervertebral disc *in vivo*. The state of differentiation would be either de-differentiated (flattened cells grown in monolayer on traditional plastic cultureware) or differentiated (rounded cells) grown in three-dimensional microenvironments such as alginate, agarose, or collagen sponges. Dr. Gruber conducted studies of the growth of annulus cells of the therapeutic composition. Dr. Gruber showed that the annulus cells of the sand rat were proliferating cells. *Declaration of Dr. Gruber, Paragraph 8, Exhibit B, Figures A and B.*

In addition, Dr. Gruber's studies show that the cultured disc cells in the therapeutic composition are secreting extracellular matrix components including collagen, as required in new Claim 37. The results are shown in Figures C-F of Exhibit B, wherein secretion of extracellular matrix components can be seen. *Declaration of Dr. Gruber, Paragraph 9, Exhibit B, Figures C-F.*

It is therefore respectfully submitted that the therapeutic composition of new Claims 35-38 meet the requirements of 35 U.S.C. §112, ¶1.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner For Patents, Washington, DC 20231, on January 7, 2002.

Janet F. Moore